



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.: 10/603,678 Confirmation No.: 3756  
Applicant(s): Feller *et al.*  
Filed: June 25, 2003  
Art Unit: 1625  
Examiner: Dentz, Bernard I.  
Title: B<sub>3</sub>-ADRENORECEPTOR AGONISTS, AGONIST COMPOSITIONS AND METHODS OF USING

Docket No.: 046295/264122  
Customer No.: 00826

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

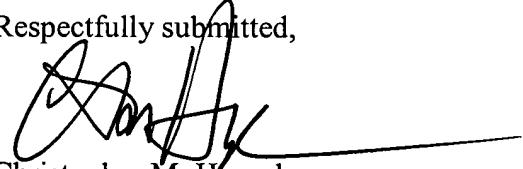
INFORMATION DISCLOSURE STATEMENT  
UNDER 37 C.F.R. § 1.97(c)

Sir:

Attached is a list of documents on form PTO-1449 together with copies of each identified document. Also enclosed is a translation or a concise explanation of each non-English language document. It is requested that the Examiner consider these documents and officially make them of record in accordance with the provisions of 37 C.F.R. § 1.97 and Section 609 of the MPEP. By submitting the listed documents, Applicant in no way makes any admission as to the prior art status of the listed documents, but is instead submitting the listed documents for the sake of full disclosure.

This Information Disclosure Statement is submitted in accordance with 37 C.F.R. § 1.97(c), before final Office Action or Allowance, whichever is earlier. A check for the \$180.00 fee specified in 37 C.F.R. § 1.17(p) is enclosed. The Commissioner is authorized to charge any additional fee, or credit any refund, to our Deposit Account No. 16-0605.

Respectfully submitted,

  
Christopher M. Humphrey  
Registration No. 43,683



In re Feller *et al.*

Appl. No.: 10/603,678

Filed: June 25, 2003

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**CUSTOMER No. 00826**

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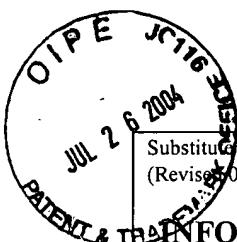
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Tracey S. Wright



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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Feller et al. Confirmation No.: To Be Assigned  
Appl No.: To Be Assigned Group Art Unit: 1625  
Filed: Concurrently herewith Examiner: Dentz, Bernard I.  
For:  $\beta_3$  - ADRENORECEPTOR AGONISTS, AGONIST COMPOSITIONS AND METHODS OF  
USING

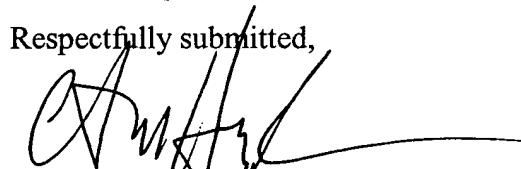
Mail Stop Patent Application  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT  
CITATION UNDER 37 C.F.R. § 1.97**

Attached is a list of documents on form PTO-1449. It is requested that the Examiner consider these documents and officially make them of record in accordance with the provisions of 37 C.F.R. § 1.97 and Section 609 of the MPEP. By submitting the listed documents, Applicant in no way makes any admission as to the prior art status of the listed documents, but is instead submitting the listed documents for the sake of full disclosure.

All items were supplied in parent Application No. 09/164,047 filed September 30, 1998. Since the benefit of this application was claimed under 35 U.S.C. 120, no copies need to be furnished in accordance with 37 C.F.R. 1.98(d); however, copies will be furnished on request.

Respectfully submitted,



Christopher M. Humphrey  
Registration No. 43,683

**Customer No. 00826**

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Tracey S. Wright

Substitute for form 1449A/PTO (Revised 10/2001)  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(Use as many sheets as necessary)</i>		<b>Complete if Known</b>			
		Application Number	To Be Assigned		
		Filing Date	To Be Assigned		
		First Named Inventor	Feller <i>et al.</i>		
		Group Art Unit	1612		
		Examiner Name	B. Dentz		
Sheet	1 of 4	Attorney Docket Number 046295/264122			
<b>U. S. PATENT DOCUMENTS</b>					
Examiner Initials*	Cite No.	Document Number Number - Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages of Relevant Figures Appear
	1	3,337,539	08-22-1967	Mészáros <i>et al.</i>	
	2	3,438,989	04-15-1969	Shavel, Jr. <i>et al.</i>	
	3	3,497,516	02-24-1970	Mashimo <i>et al.</i>	
	4	3,647,799	03-07-1972	Watanabe <i>et al.</i>	
	5	3,818,015	06-18-1974	Yamato <i>et al.</i>	
	6	3,872,130	03-18-1975	Kreighbaum <i>et al.</i>	
	7	3,873,704	03-25-1975	Yamato <i>et al.</i>	
	8	3,910,915	10-07-1975	Yonan	
	9	3,910,927	10-07-1975	Kreighbaum <i>et al.</i>	
	10	3,988,339	10-26-1976	Kaiser <i>et al.</i>	
	11	4,054,659	10-18-1977	Ikezaki <i>et al.</i>	
	12	4,321,254	03-23-1982	Ali	
	13	4,442,108	04-10-1984	Le Polles <i>et al.</i>	
	14	4,525,589	06-25-1985	Hidaka <i>et al.</i>	
	15	4,536,510	08-20-1985	Wasserman <i>et al.</i>	
	16	4,666,918	05-19-1987	Ivanova <i>et al.</i>	
	17	4,707,485	11-17-1987	Kaiser <i>et al.</i>	
	18	4,737,504	04-12-1988	Miller <i>et al.</i>	
	19	4,798,897	01-17-1989	Hidaka <i>et al.</i>	
	20	4,812,573	03-14-1989	Durant <i>et al.</i>	
	21	4,857,301	08-15-1989	Czarniecki <i>et al.</i>	
	22	5,059,608	10-22-1991	Takasugi <i>et al.</i>	
	23	5,177,085	01-05-1993	Naef	
	24	5,210,088	05-11-1993	Minchin <i>et al.</i>	
	25	5,238,935	08-24-1993	Dugar <i>et al.</i>	
	26	5,246,943	09-21-1993	Blankley <i>et al.</i>	
Examiner Signature		Date Considered			

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet **2** of **4**

Complete if Known	
Application Number	To Be Assigned
Filing Date	To Be Assigned
First Named Inventor	Feller <i>et al.</i>
Group Art Unit	1612
Examiner Name	B. Dentz
Attorney Docket Number	046295/264122

### U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No.	Document Number Number - Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages of Relevant Figures Appear
	27	5,272,270	12-21-1993	Hirsenkorn <i>et al.</i>	
	28	5,340,811	08-23-1994	Kajihara <i>et al.</i>	
	29	5,350,757	09-27-1994	Blankley <i>et al.</i>	
	30	5,362,736	11-08-1994	Ishikawa <i>et al.</i>	
	31	5,446,164	08-29-1995	Ishikawa <i>et al.</i>	
	32	5,498,717	03-12-1996	Ishikawa <i>et al.</i>	
	33	5,519,034	05-21-1996	Kozlik <i>et al.</i>	
	34	5,525,614	06-11-1996	Blankley <i>et al.</i>	
	35	5,707,985	01-13-1998	McKenzie <i>et al.</i>	
	36	5,750,520	05-12-1998	Danilewicz <i>et al.</i>	
	37	5,756,516	05-26-1998	Liu <i>et al.</i>	
	38	5,798,352	08-25-1998	Danilewicz	
	39	5,804,586	09-08-1998	Sargent <i>et al.</i>	
	40	5,807,868	09-15-1998	Sargent <i>et al.</i>	
	41	5,880,285	03-09-1999	Broger <i>et al.</i>	
	42	5,929,085	07-27-1999	MacDonald <i>et al.</i>	
	43	6,043,253	03-28-2000	Brockunier <i>et al.</i>	
	44	6,063,925	05-16-2000	Demian <i>et al.</i>	
	45	6,127,381	10-03-2000	Basu <i>et al.</i>	
	46	6,153,608	11-28-2000	Hidaka <i>et al.</i>	
	47	6,248,754	06-19-2001	Coulton <i>et al.</i>	
	48	6,274,594	08-14-2001	Coulton <i>et al.</i>	
	49	6,277,861	08-21-2001	Harling <i>et al.</i>	
	50	US 2001/0039289 A1	11-08-2001	Blok <i>et al.</i>	

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Substitute for form 1449A/PTO (Revised 10/2001)				Complete if Known	
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				First Named Inventor	Feller <i>et al.</i>
				Group Art Unit	1612
				Examiner Name	B. Dentz
Sheet	3	of	4	Attorney Docket Number	046295/264122

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Examiner Initials*	Cite No.	Document Number Number - Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages of Relevant Figures Appear
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#### FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.	Foreign Patent Document Country Code - Number Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
	51	JP 47018898	09-18-1972	Japan Chemipha Co., Ltd.	Abstract	
	52	JP 52095676	08-11-1977	Dainippon Pharmaceutical Co., Ltd.	Abstract	
	53	EP 0 210 827 A2	02-04-1987	Smithkline Beckman Corporation		
	54	WO 99/44609 A1	09-10-1999	Merck & Co., Inc.		

#### OTHER DOCUMENTS

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T
	55	CHRISTOFF, <i>et al.</i> , "Synthesis and Evaluation of Trimetoquinol Derivatives: Novel Thromboxane A <sub>2</sub> /Prostaglandin H <sub>2</sub> Antagonists with Diminished β-Adrenergic Agonist Activity", <i>J. Med. Chem.</i> , 1997, Vol. 40, pp. 85-91.	
	56	DE LOS ANGELES, <i>et al.</i> , "Iodinated Analogs of Trimetoquinol as Highly Potent and Selective β <sub>2</sub> -Adrenoceptor Ligands", <i>J. Med. Chem.</i> , 1996, Vol. 39, pp. 3701-3711.	
	57	HE, <i>et al.</i> , "Synthesis and Human β-Adrenoceptor Activity of 1,2,3,4-Tetrahydroisoquinoline-6-ol Derivatives, In Vitro", <i>Am. Chem. Soc.</i> , 218 <sup>th</sup> ACS National Meeting, August 22-26, 1999, Abstract.	
	58	ISHIWATA, <i>et al.</i> , "Syntheses of Aminoisoquinolines and Related Compounds. VI. A Modified Synthesis of dl-pronuciferine", <i>Chem. Pharm. Bull.</i> , 1970, Vol. 18(6), Abstract.	
	59	ISHIWATA, <i>et al.</i> , "Syntheses of Aminoisoquinolines and Related Compounds. II. Syntheses of 6-amino-1-benzylisoquinolines by the Bischler-Napieralski reaction", <i>Chem. Pharm. Bull.</i> , 1969, Vol. 17(11), Abstract.	
	60	ISHIWATA, <i>et al.</i> , "Synthesis of Aminoisoquinolines and Related Compounds. IX. Synthesis of (+)-0-methylcaseadine", <i>Chem. Pharm. Bull.</i> , 1970, Vol. 18(9), Abstract	
	61	MEMETZIDIS, <i>et al.</i> , "Synthesis of Aromatic Chloroberbines", <i>Heterocycles</i> , 1990, Vol. 31(2), Abstract.	
	62	NIKULIN <i>et al.</i> , "A Shortened Approach to Parallel Synthesis of Tetrahydroisoquinolines (THI) Via Bishler-Napieralski Cyclization", <i>Am. Chem. Soc.</i> , 215 <sup>th</sup> ACS National Meeting, March 29-April 2, 1998.	
	63	ZHENG, <i>et al.</i> , "2-Amino-4-Aryl-4,5,6,7-Tetrahydrothiazolo[5,4-c]Pyridines: Proposed Novel Catechol Bioisosteric Analogs of Trimetoquinol (TMQ) – A Potent β-Adrenoceptor Agonist and TP Receptor Antagonist", <i>Am. Chem. Soc.</i> , 1995 Joint Southeast-Southwest Regional Meeting, November 29 – December 1, 1995, Abstract.	
Examiner Signature		Date Considered	

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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 4 of 4

### Complete if Known

Application Number	To Be Assigned
Filing Date	To Be Assigned
First Named Inventor	Feller et al.
Group Art Unit	1612
Examiner Name	Dentz

Attorney Docket Number 046295/264122

### OTHER DOCUMENTS

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s) , volume-issue number(s), publisher, city and/or country where published.	T
	64	ADEJARE, et al., "Syntheses and $\beta$ -Adrenergic Agonist and Antiaggregatory Properties of N-Substituted Trimetoquinol Analogues", <i>J. Med. Chem.</i> , 1986, pp. 1603-1609, Vol. 29.	
	65	AWN, et al., "Characterization of the Inhibition of U46619-Mediated Human Platelet Activation by the Trimetoquinol Isomers", <i>Biochemical Pharmacology</i> , 1988, pp. 3023-3033, Vol. 37, No. 15.	
	66	CLARK, et al., "5-Fluoro- and 8-Fluorotrimetoquinol: Selective $\beta_2$ -Adrenoceptor Agonists", <i>J. Med. Chem.</i> , 1987, pp. 86-90, Vol. 30.	
	67	FRAUNDORFER, et al., "Biochemical and Pharmacological Characterization of High-Affinity Trimetoquinol Analogs on Guinea Pig and Human Beta Adrenergic Receptor Subtypes: Evidence for Partial Agonism <sup>1</sup> ", <i>J. Pharmacology and Experimental Therapeutics</i> , 1994, pp. 665-674, Vol. 270, No. 2.	
	68	FRAUNDORFER, Paul F., "Functional and Biochemical Characterization of Trimetoquinol (TMQ) Analog Interactions with $\beta$ -Adrenergic Receptor Subtypes", A Dissertation, The Ohio State University, 1993.	
	69	HARROLD, et al., "Synthesis and Platelet Antiaggregatory Activity of Trimetoquinol Analogs as Endoperoxide/Thromboxane A <sub>2</sub> Antagonists", <i>Drug Design and Delivery</i> , 1987, pp. 193-207, Vol. 1.	
	70	HOWE, Ralph, " $\beta_3$ -Adrenergic agonists", <i>Drugs of the Future</i> , 1993, pp. 529-549, Vol. 18, No. 6.	
	71	IWASAWA, et al., "Studies on Tetrahydroisoquinolines (THI) (I) Bronchodilator Activity and Structure-Activity Relationship", <i>Jap. J. Pharmacol.</i> , 1967, pp. 143-152, Vol. 17.	
	72	KAJIGAESHI, et al., "Halogenation Using Quaternary Ammonium Polyhalides. VII. <sup>1</sup> Iodination of Aromatic Amines by Use of Benzyltrimethylammonium Dichloroiodate(1-)", <i>Bull. Chem. Soc. Jpn.</i> , 1988, pp. 600-602, Vol. 61, No. 2.	
	73	MAYO, et al., "Stereo-Dependent Inhibition of Human Platelet Function by the Optical Isomers of Trimetoquinol", <i>Biochemical Pharmacology</i> , 1981, pp. 2237-2241, Vol. 30, No. 16.	
	74	SHIN, et al., "Interactions of Nonprostanoid Trimetoquinol Analogs with Thromboxane A <sub>2</sub> /Prostaglandin H <sub>2</sub> Receptors in Human Platelets, Rat Vascular Endothelial Cells and Rat Vascular Smooth Muscle Cells <sup>1</sup> ", <i>J. Pharmacology and Experimental Therapeutics</i> , 1993, pp. 1017-1023, Vol. 267, No. 3.	
	75	SHIN, et al., "Pharmacologic Antagonism of Thromboxane A <sub>2</sub> Receptors by Trimetoquinol Analogs In Vitro and In Vivo", <i>Chirality</i> , 1991, pp. 112-117, Vol. 3.	
	76	SHIN, et al., "Stereospecific Interactions of Nonprostanoid Trimetoquinol Analogs With Thromboxane A <sub>2</sub> /Prostaglandin H <sub>2</sub> Receptor Sites in Human and Rat Platelets, and Rat Vascular Endothelial and Smooth Muscle Cells", <i>Pharmacology Communications</i> , 1992, pp. 303-312, Vol. 1, No. 4.	
	77	YAMATO, et al., "Synthesis of 6,7-Dihydroxy-1,2,3,4-Tetrahydroisoquinoline Derivatives", <i>Tetrahedron</i> , 1966, pp. 129-134, Suppl. 8, Part 1.	

RTA 2138723v1

Examiner Signature	Date Considered
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Commissioner for Patents  
P.O. Box 1450

Date Mailed: 06/25/2003

Alexandria, VA 22313-1450 Atty. Dkt. No. 046295/264122  
Kindly acknowledge receipt of the accompanying CONTINUATION PATENT  
APPLICATION with Application Transmittal Cover Sheet for:

Inventor(s): Feller *et al.*

Title of Invention: **β3-ADRENOCEPTOR AGONISTS, AGONIST  
COMPOSITIONS AND METHODS OF USING**

Pages of Spec. (including claims and abstract) 113; No. of Claims 52

Declaration Enclosed x (2 pages); IDS with PTO 1449 Enclosed x ;

Other Documents: 1. Preliminary Amendment (3 pages)

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Humphrey

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